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L1 3289 S MCP OR (MONOCYTE (1W) CHEMOTACTIC (1W) PROTEIN)
L2 196 S L1 (P) ANTAGONIST?
L3 14 S L2 (P) TRUNCAT?
L4 630 S (MONOCYTE (1W) CHEMOTACTIC (1W) PROTEIN)
L5 102 S L4 AND ANTAGONIST
L6 4 S L5 AND TRUNCAT?

FILE 'CAPLUS, EMBASE, BIOSIS' ENTERED AT 14:31:26 ON 12 JUN 2001

L7 245 S L5
L8 7 S L6

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L3 ANSWER 4 OF 14 MEDLINE

AB Chemokines are important mediators in infection and inflammation. The **monocyte chemotactic proteins (MCPs)** form a subclass of structurally related C-C chemokines. **MCPs** select specific target cells due to binding to a distinct set of chemokine receptors. Recombinant and synthetic **MCP-1** variants have been shown to function as chemokine **antagonists**. In this study, posttranslationally modified immunoreactive **MCP-1** and **MCP-2** were isolated from mononuclear cells. Natural forms of **MCP-1** and **MCP-2** were biochemically identified by Edman degradation and mass spectrometry and functionally characterized in chemotaxis and Ca²⁺-mobilization assays. Glycosylated **MCP-1** (12 and 13.5 kDa) was found to be two- to threefold less chemotactic for monocytes and THP-1 cells than nonglycosylated **MCP-1** (10 kDa). Natural, NH₂-terminally **truncated MCP-1(5-76)** and **MCP-1(6-76)** were practically devoid of bioactivity, whereas COOH-terminally processed **MCP-1(1-69)** fully retained its chemotactic and Ca²⁺-inducing capacity. The capability of naturally modified **MCP-1** forms to desensitize the Ca²⁺ response induced by intact **MCP-1** in THP-1 cells correlated with their agonistic potency. In contrast, naturally modified **MCP-2(6-76)** was devoid of activity, but could completely block the chemotactic effect of intact **MCP-2** as well as that of **MCP-1**, **MCP-3**, and **RANTES**. Carboxyl-terminally processed **MCP-2(1-74)** did retain its chemotactic potency. Although comparable as a chemoattractant, natural intact **MCP-2** was found to be 10-fold less potent than **MCP-1** in inducing an intracellular Ca²⁺ increase. It can be concluded that under physiologic or pathologic conditions, posttranslational modification affects chemokine potency and that natural **MCP-2(6-76)** is a functional C-C chemokine inhibitor that might be useful as an inhibitor of inflammation.

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AUTHOR: Proost P; Struyf S; Couvreur M; Lenaerts J P; Conings R; Menten P; Verhaert P; Wuyts A; Van Damme J

CORPORATE SOURCE: Rega Institute for Medical Research, Laboratory of Molecular Immunology, University of Leuven, Belgium.

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